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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,715	09/29/2003	Harry A. Dugger III	N9810.0025/P025	9275

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/671,715	DUGGER ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/20/06 AND 12/21/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,22-26,28,40-46,48,57,59 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,22-26,28,40-46,48,57,59 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Amendments and Remarks filed on 11/20/06 and an IDS filed on 12/21/06. Claims 1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61 have been amended while claims 9, 11-21, 27, 29-39, 47, 49-56, 58, 60 and 62 have been cancelled. No new claims have been added. Accordingly claims **1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61** are pending.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deihl (WO 9413280) in view of Fassberg et al (EP 0656206A1) and further in view of Kanios et al (5,719,197).

Deihl teaches a **sprayable analgesic** composition comprising an analgesic compound which is absorbed into the bloodstream through the **buccal mucosa** and a pharmacologically acceptable liquid carrier. In a preferred embodiment the active agent is ibuprofen and the liquid carrier is **aqueous ethanol** (see page 3). The formulation may also contain other ingredients such as surfactants, humectants, **flavoring agents**, etc (see page 4). The table in example I shows the concentration ranges of each

ingredient. Deihl fails to disclose other suitable active agents for the said formulation, or the use of other solvents including polyethylene glycol and non-polar solvent.

Fassberg discloses aerosol, formulations for oral or nasal administration, which comprise a medicament, an excipient, propellant and optionally surfactants. The suitable excipients include **alcohols, polyethylene glycols, short chain fatty acids**, etc (see page 3). Fassberg discloses that any pharmaceutically active agent which can be delivered by oral or nasal inhalation may be used. Examples include antihistamines, antiallergics, analgesics, antibiotics, steroids, bronchodilators, etc (see page 5, lines 42-50).

Kanios teaches compositions and methods for topical administration of pharmaceutically active agents. Topical administration means a direct contact of the formulation with tissue, such as skin or membrane, particularly the oral or **buccal mucosa** (col. 1, lines 29-59).

Kanios discloses that the composition comprises a therapeutically effective amount of at least one pharmaceutically **active agent**, a pharmaceutically acceptable **solvent** for the active agent (col. 2, lines 22-28). The solvent is preferably a polyhydric alcohol such as polypropylene glycol, ethylene glycol, also solvents including fatty acids such as oleic acid, as well as fatty esters or alcohols. The solvent is present in an amount from about 20 to 50 weight percent based on the total weight of the composition (col. 4, lines 1-49; col. 5, lines 24-66). The concentration of the solubilized active agent can range from **1 to 50%** by weight (col. 8, lines 1-9). The acceptable carrier is intended

to be any suitable finite or non-finite carrier including liquids, semi-liquids or solid carriers. Thus the active agent may be admixed with carriers such as spray-solution or any non-finite carrier known in the art for delivery of active agents (col. 8, lines 54-67). Other additives may be incorporated into the formulations such as flavorings (col. 10, lines 48-56).

Kanios discloses that pharmaceutically active agents suitable for such formulation include galanthamine, lidocaine, mepivacaine, atracurium, ipratropium, amantadine, diazepam, pregabalin, primidone, clozapine, chlorpromazine, haloperidol, amitryptiline, buspirone, chlorzoxazone, cyclobenzaprine, interferon beta, estradiol, nimodipine, tacrine, carbidopa, acetylcholine, epinephrine, pergolide, doxepine, clomipramine, **zolpidem,** amphetamine, dextroamphetamine, methylphenidate, sumatriptan, pemoline, mazindol, desipramine, flumazenil, mesoridazine, etc (columns13-31).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of formulations for buccal mucosal administration of Diehl, to have looked in the art for other specific solvents suitable for spray formulations of liquid carriers, as taught by Fassberg et al, with reasonable expectations of successfully preparing suitable formulations for various therapies. Furthermore it is obvious to one of ordinary skill in the art to have substituted any suitable active agent for the active agents of Diehl's buccal spray formulations as claimed as taught by Kanios et al.

Claims 1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu et al (WO 9303751) in view of Kanios et al (5,719,197).

Fu teaches compositions and methods for the sublingual or buccal administration of therapeutic agents. The compositions comprise a therapeutic agent dissolved or dispersed in a carrier which comprises a solvent, an optional cosolvent, and an oral mucosal membrane transport enhancing agent. The solvent comprises from about 50% w/v to about 95% w/v of the carrier of a non-toxic alcohol. Non-alcohols useful in the said formulations include ethanol, isopropanol, stearyl alcohol, propylene glycol, polyethylene glycol and the like. Most preferred alcohol is ethanol. The cosolvent is selected from water (page 4, lines 12-26). Essential or volatile oils such as peppermint oil, spearmint oil, menthol, etc, are added in a concentration of between about 1 and 5% w/v (page 5, lines 4-10). The said liquid compositions are formulated in a liquid spray or a liquid drop (page 6, lines 1-2). Fu et al lacks teachings on zolpidem.

Kanios, discussed above, teaches formulations comprising active agents such as zolpidem and liquid carriers.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of formulations for buccal mucosal administration of Fu et al, to have looked in the art for other specific active agents suitable for spray formulations of liquid carriers, as taught by Knaios, with reasonable

expectations of successfully preparing suitable formulations for various therapies. Furthermore it is obvious to one of ordinary skill in the art to have substituted any suitable active agent for the active agents of Fu et al's buccal spray formulations as taught by Kanios.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61** are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31, 64-91 and 124-134 of co-pending Application No. 10/230,060. The double patenting rejection is proper because the examined claims and the reference claims are substantially the same. The difference is that claims of the co-pending

Application '060 recite a broader scope of active agents which includes sedatives such as zolpidem. Thus the instant claims are anticipated by the reference claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **1-8, 10, 22-26, 28, 40-46, 48, 57, 59 and 61** are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-34, 54-59 and 80-82 of co-pending Application No. 09/537,118 in view of Kanios. The double patenting rejection is proper because the examined claims and the reference claims are substantially the same. The difference is that claims of the co-pending Application '118 do not recite zolpidem as the active agents. However, kanios teaches formulations comprising active agents such as zolpidem. Thus it would have been obvious to one of ordinary skill in the art to have replaced the active agents of the co-pending Application '118 with the sedative zolpidem as taught by Kanios to provide a new dosage form and a new option for treating insomnia.

Pertinent Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Oguri et al (JP 02-026661) teaches formulations for aerosol delivery comprising an active agent and a liquid carrier. Suitable active agents include analgesics and carrier formulations include polar and non-polar solvents and other agents. Carrier formulations may comprise a mixture of a polar and a non-polar solvent.

Polar solvents include water, alcohols such as ethyl alcohol, propylene glycols. Non-polar solvents include hydrocarbons or halogenated hydrocarbons are suitable. Menthol is one of flavoring agents used.

Response to Arguments

Applicant's arguments filed 11/20/06 have been fully considered but they are not persuasive.

Applicant argues that Deihl would not have been considered a credible or relevant teaching because "each spray is 50 microliters and contains 1 milligram of acetaminophen or ibuprofen. This treatment is repeated once after five minutes. That is, Deihl teaches a total dose of 4-8 milligrams of acetaminophen or ibuprofen". Applicant however agrees that that "Deihl purports to teach a sprayable analgesic composition where an analgesic is capable of being absorbed into bloodstream through the buccal mucosa" and that compositions comprise acetaminophen or ibuprofen in an aqueous ethanol base. This is not commensurate with the scope of claims. Claims are drawn to a method of **administering** zolpidem comprising spraying the oral mucosa a composition comprising zolpidem in an amount between 0.001 and 60% and a polar solvent in an amount between 30 and 99.69% both by weight of the composition. The formulation exemplified by Deihl (example 1) comprises about 1.93% acetaminophen and about 51.87% a polar solvent mix of ethanol and water. Thus Deihl is clearly teaching a composition comprising an active agent and the polar solvent in amounts that overlaps the required amounts in the instant claims. Deihl teaches and Applicant agrees, delivery

of the said sprayable formulation to the oral mucosa for absorption through the buccal mucosa. References such as Fassberg, Kanios or Drug Facts and Comaprison have been employed to show that formulations such as those taught by Deihl may include any pharmaceutically active agent. Thus it has been established that Deihl in view of the cited references has clearly met the instant claims. In other words Applicant's arguments are not commensurate with the scope of claims because instant claims do not require any therapeutic dosage, a percent bioavailability or degree of effectiveness.

Applicant argues that according to Remington, 19th ed. "when only small amounts of drugs are required to gain access to the blood, the buccal route may be satisfactory, providing the physicochemical prerequisites for absorption by this route are present in the drug and dosage form. Only a few drugs may be given successfully by this route". This is neither persuasive nor commensurate with the scope of claims. Various references e.g. Deihl, Fassberg and Cassidy et al, 1993, *Controlled buccal delivery of buprenorphine* (copy provided) have shown that many different active agents such as analgesics, polypeptides, antibiotics, etc, can successfully be administered to the buccal mucosa. Also there is no criticality disclosed by the Applicant in spraying zolpidem to the oral mucosa. In fact as seen in cited references and many co-pending applications, it is obvious that different active agents can be included in the same formulation base and successfully sprayed in the oral mucosa. Therefore substituting different active agents in the same solvent formulation is an obvious variation and does not alter the scope of the claim.

Applicant argues that Fassberg is related to an inhalation aerosol comprising a propellant and does not disclose a method of delivery of a propellant-free spray to the buccal mucosa. Applicant also argues that kanios teaches an intermediate composition that is made into a "finished dosage form" by applying a flexible backing, and that Kanios does not teach buccal spray method of administration. While Applicant's statements here are correct, the arguments are not persuasive. Fassberg and Kanios are supplementary art to provide teachings on what is missing in the primary art. Fassberg and Kanios teach solution formulations comprising various active agents, solvents and excipients and one of ordinary skill in the art would be motivated to combine the said solvents and active agents to improve on the stability, delivery or effectiveness of the formulations.

Applicant argues that Fu et al teaches compositions for sublingual delivery of specific polypeptides and in the presence of a permeation enhancer. This is not persuasive because Fu teaches sublingual delivery of formulations comprising a therapeutic agent, particularly polypeptides. Also it is noted that instant formulations employ the open-ended language of "comprising" and do not exclude permeation enhancers. Thus presence or absence of the permeation enhancers is not relevant to the examination of instant claims here.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mina Haghighatian
February 09, 2007

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